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DEPARTMENT OF MOLECULAR BIOPHYSICS
AND BIOCHEMISTRY

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May 22, 1978

Dr. Joshua Lederberg
Department of Genetics
School of Medicine
Stanford University
Stanford, California 94305

Dear Josh:

Although you must be inundated with unsolicited advice for RU, let me nevertheless toss my own into the hopper. Probably you would agree with the premise that development is the central and most germinal problem in biology today. I find it helpful to divide the problem into two sequential domains, the first involving the establishment of the developmental program, and the second the expression of the program. This division is perhaps most clearly seen in *Drosophila*, in which the transition occurs at the blastula stage. During oogenesis, the developmental program is generated as a two-dimensional epigenetic pattern in the oocyte, and afterwards the program becomes irreversibly fixed at the cellular level when cell boundaries are demarcated in the blastula. This phase, as you know, is still virtually a total mystery, the oocyte remaining a black box. I expect the situation will change dramatically soon as new techniques are exploited, particularly gene cloning and antibody cloning, which are ideally suited for this purpose.

The subsequent expression of the developmental program appears to involve both constitutive gene functions and inducible gene functions that respond to extracellular signals, such as cell-cell surface interactions and hormones. Recently, I have become interested in the developmental role of hormonal signals, particularly of steroid hormones as exemplified by ecdysone in *Drosophila*. I have enclosed a reprint of our initial foray into the field. What has impressed me about ecdysone, and I expect this applies to steroid hormones in general, is its involvement in almost all aspects of development and adult functions. Apparently, nature has chosen to use a ubiquitous simple signal for the large variety of different responses. Specificity is achieved by changes in hormone titer during development, which allows for different responses at different times in the same tissue, and by tissue-specific receptors which allow for different responses at the same time in different tissues. There is not much known about any of the three principal aspects of steroid hormones, either regulation, biosynthesis or response. One of the attractions of the problem is the likelihood that the basic mechanisms are general for all eucaryotes.

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This glib overview of a complex topic is intended to bring to your attention the possibility of establishing at RU a section, that might be called Developmental Endocrinology, composed of three laboratories, one interested in basic mechanisms probably best studied in *Drosophila*, another in mammalian aspects for which the mouse should be the best organism, and a third clinically oriented towards human diseases resulting from steroid hormone malfunctions. A tripartite section of this kind could be truly complementary, in view of the commality of biological effects involved with all steroid hormones.

If this approach interests you, we could discuss it further after you and your family have resettled.

Cordially,

A handwritten signature in cursive script, appearing to read "Alan".

Alan Garen

AG:m1
Encl.